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Hybrid-DFT study and NBO interpretations of conformational behaviors of 2-methoxy-1,2,4,5-tetrahydro-benzo[*d*]oxepine, -thiepine and -selenepine

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Abstract

NBO analysis and density functional theory (DFT: B3LYP/6-311+G**) based method were used to study the impacts of the *anomeric effects* (*AE*) on the conformational properties of 2-methoxy-1,2,4,5-tetrahydro-benzo[*d*]oxepine (**1**), -thiepine (**2**) and -selenepine (**3**). The Gibbs free energy difference (G_{eq}–G_{ax}) values (i.e. ΔG_{eq-ax}) at 298.15 K and 1 atm between the axial and equatorial conformations increase from compound **1** to compound **2** but decrease from compound **2** to compound **3**. The NBO analysis showed that the *AE* associated with donor-acceptor (LP→σ*) interactions increases from compound **1** to compound **2** but decreases from compound **2** to compound **3**. Also, the calculated dipole moment difference [$\Delta(\mu_{eq} - \mu_{ax})$] values between the axial and equatorial conformations increase from compound **1** to compound **2** but increase from compound **2** to compound **3**. Based on the results obtained, there is no conflict between the *AE* and the electrostatic interactions [i.e. $\Delta(\mu_{eq} - \mu_{ax})$] on the conformational behaviors of compounds **1**-**3**.

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1. Introduction

In 1955, Edward proposed that alkoxy groups at C_1 in pyranose rings are generally more stable in the axial rather than in the equatorial configuration [1]. This proposal invokes an unfavorable disposition of the unshared electrons of the ring oxygen and the C_1-O polar bond. It is appropriate to point out that this explanation may be the first reference to the importance of lone electron-pair orientation on conformational stability.

Since the preferred geometry of many molecules can be viewed as the result of the maximization of an interaction between the best donor lone pair and the best acceptor bond [2], the stereoelectronic interactions are expected to play an important role in the conformational properties of heterocyclic compounds [3, 4]. The most dominant conformation-controlling factor in carbohydrate and heterocyclic compounds is known as the *anomeric effect* (*AE*) [5]. It should

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be noted that the *AE* is in favour of the axial conformation of a six-membered saturated ring in opposition to the steric effect which normally leads to a preference for the equatorial conformation. In this context, there is a stereoelectronic preference for conformations in which the best donor lone pair is antiperiplanar to the best acceptor bond [6]. The *AE* in six membered saturated heterocyclic compounds must be considered as the difference between the sum of the *endo-AE* and *exo-AE* in the equatorial conformer and the same sum for the axial conformer [6] (Euation 1).

$$anomeric\ effect = \sum(endo\text{-}AE_{eq}+ exo\text{-}AE_{eq}) - \sum(endo\text{-}AE_{ax} + exo\text{-}AE_{ax}) \quad \text{(Eq. 1)}$$

In 1992, Désilets and St-Jacques reported the results of a low-temperature ^{1}H and ^{13}C high-field NMR spectroscopy of six thio derivatives of benzocycloheptane in solution.[7] Their results demonstrated the predominance of the axial chair conformation in these compounds that argues in favor of a strong *AE* [7].

Although the importance of the LP→σ* electron delocalization in seven membered sulfur-containing heterocycles has investigated [6-12] there is insufficient published experimental information about the stereoelctronic interactions in compound **1** [7] and also there is no published experimental or quantitative theoretical data about the donor-acceptor delocalization effects on the conformational properties of compounds **1-3**. In this work, the impacts of the stereoelectronic interactions associated with the *AE*, electrostatic and steric interactions on the conformational and structural properties of compounds **1-3** were investigated computationally using hybrid-DFT based methods and natural bond orbital (NBO) analysis (see Scheme 1) [8-13].

1: X=F, **2**: X=Cl, **3**: X=Br
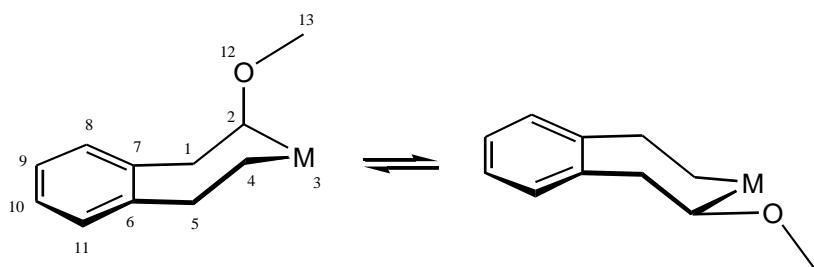
Scheme 1 Schematic representation of conformations of compounds **1-6**.

2. Computational details

Hybrid DFT calculations were carried out using the B3LYP/6-311+G** levels of theory with the GAUSSIAN 03 package of programs.[8] The energy minimization of these compounds was carried out only for the axial and equatorial position of methoxy groups on the chair conformations of the heterocyclic 1,2,4,5-tetrahydro-benzo[*d*]oxepine (**1**), -thiepine (**2**) and -selenepine (**3**) rings.

An NBO analysis was then performed for the axial and equatorial conformations of compounds **1-6** by the NBO 5.G program contained in the PC-GAMESS interface [13]. The bonding and antibonding orbital occupancies in the axial and equatorial conformations of compounds **1-3,** and also the stabilization energies associated with *endo-AEs* and *exo-AEs* were calculated using NBO analysis. The LP→σ* resonance energies are proportional to $S^2/\Delta E$ where S is the orbital overlap and ΔE is the energy differences between the LP and σ* orbitals [14, 15]:

$$Stabilization\ or\ resonance\ energy\ \alpha\ (S^2/\Delta E)$$

In addition, the stabilization energy (E_2) associated with $i{\rightarrow}j$ delocalization, is explicitly estimated by the following equation:

$$E_2 = q_i \frac{F^2(i,j)}{\varepsilon_j - \varepsilon_i}$$

where q_i is the ith donor orbital occupancy, ε_i, ε_j are diagonal elements (orbital energies) and $F(i,j)$ off-diagonal elements, respectively, associated with the NBO Fock matrix. Therefore, there is a direct relationship between $F(i,j)$ off-diagonal elements and the orbital overlap (S).

The stabilization energies (E_2) associated with $LP_{ax}M_3{\rightarrow}\sigma^*_{C2-O12}$, $LP_{eq}M_3{\rightarrow}\sigma^*_{C2-O12}$ (*endo-AE*), $LP_1O_{12}{\rightarrow}\sigma^*_{C2-M3}$, $LP_2O_{12}{\rightarrow}\sigma^*_{C2-M3}$ (*exo-AE*) electron delocalizations (see Figs. 1, 2) and their influences on the conformational properties of compounds **1-3** were quantitatively investigated by the NBO analysis [13]. It has to be noted that the NBO analysis is a sufficient approach to investigate the stereoelctronic interactions on the reactivity and dynamic behaviors of chemical compounds [16-23].


$LP_{ax}M_3{\rightarrow}\sigma^*_{C2-O12}$ $LP_2O_{12}{\rightarrow}\sigma^*_{C2-M3}$
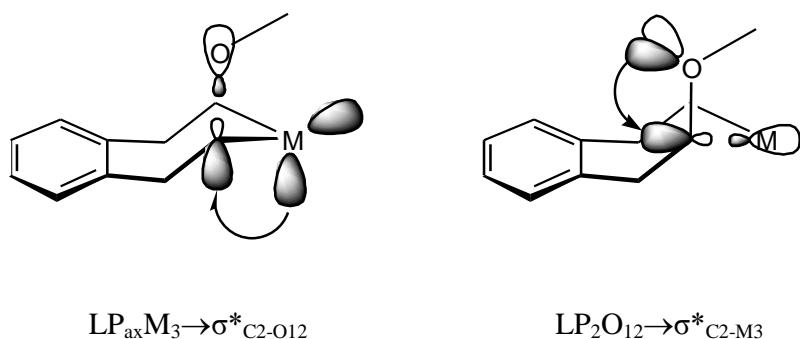
Fig. 1. Schematic representation of the electron delocalization between non-bonding and anti-bonding orbitals ($LP_{ax}M_3{\rightarrow}\sigma^*_{C2-O12}$, $LP_2O_{12}{\rightarrow}\sigma^*_{C2-M3}$) in compounds **1-3**.
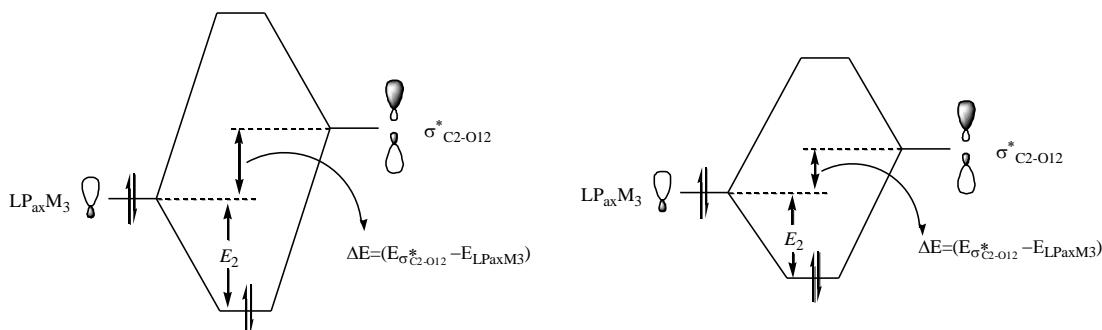
Fig. 2. Schematic representation of second order perturbation energy associated with $LP_{ax}M_3{\rightarrow}\sigma^*_{C2-O12}$, $LP_2O_{12}{\rightarrow}\sigma^*_{C2-M3}$ electron delocalizations in compounds **1-3**.

3. Results and Discussion

3.1. Conformation preference

The Gibbs free energy, enthalpy and entropy differences (i.e. ΔG, ΔH and ΔS) for the axial and equatorial conformations of compounds **1-3**, as calculated at the B3LYP/6-311+G** level of theory are given in Table 1. The calculated Gibbs free energy difference ($G_{eq}-G_{ax}$) values between the axial and equatorial conformations (i.e. ΔG_{eq-ax}) of compounds **1-3** are -0.13, 5.72 and 1.93 kcal mol^{-1}, as calculated at the B3LYP/6-311+G** level of theory, respectively (see

Table 1). Based on the results obtained, the equatorial conformation of compound **1** is more stable than its axial conformation but a reverse trend observed for compound **2**. There is a strong axial preference for compound **2**. The axial preference in compound **2** is less than that of compound **2**. Accordingly, the axial preference strongly increases from compound **1** to compound **2** but decreases from compound **2** to compound **3**.

Table 1

B3LYP/6-311+G** calculated thermodynamic functions [enthalpies, Gibbs free energies (in hartree) and entropies (in cal mol^{-1}K^{-1})] for the axial and equatorial conformations of the chair forms of compounds **1-3**.

	H(Hartree)	S(cal mol^{-1}K^{-1})	G(Hartree)	ΔH^a(Hartree)	ΔS^a (calmol^{-1}K^{-1})	ΔG^a (Hartree)
1-Eq	-577.951123	103.908	-578.000493	0.000000 (0.00)^b	0.000	0.000000 (0.00)^b
1-Ax	-577.950835	104.064	-578.000279	0.000288 (0.18)^b	0.156	0.000214 (0.13)^b
2-Eq	-900.917559	108.237	-900.968985	0.009255 (5.81)^b	0.31	0.009109 (5.72)^b
2 -Ax	-900.926814	107.927	-900.978094	0.000000 (0.00)^b	0.000	0.000000 (0.00)^b
3-Eq	-2904.256633	111.741	-	0.001905 (1.20)^b	0.969	0.001444 (0.91)^b
3 -Ax	-2904.258538	110.772	-	0.000000 (0.00)^b	0.000	0.000000 (0.00)^b

^{a} Relative to the ground state. ^{b} Numbers in parenthesis are in kcal mol^{-1}.

3.2. Stabilization energies

The *AE* associated with donor-acceptor electron delocalizations may affect the conformational behaviors of compounds **1-3**. Based on the optimized ground state geometries using the B3LYP/6-311+G** method, the NBO analysis of donor-acceptor (bond-antibond) interactions showed that the stabilization energies associated with $LP_{ax}M_3{\rightarrow}\sigma^*_{C2-X}$ delocalizations (*endo-AE*) for the axial conformations of compounds **1-3** are 11.26, 8.83 and 6.90 kcal mol^{-1}, respectively (see Table 2). Also, the stabilization energies associated with $LP_{eq}M_3{\rightarrow}\sigma^*_{C2-X}$ delocalizations (*endo-AE*) for the axial conformations of compounds **1-3** are 1.45, 0.77 and 0.58 kcal mol^{-1}, respectively. The stabilization energy associated with $LP_{ax}M_3{\rightarrow}\sigma^*_{C2-X}$ delocalizations (*endo-AE*) for the equatorial conformation of compound **1** is 1.39 kcal mol^{-1} while there is not this kind of electronic delocalizations for the equatorial conformations of compounds **2** and **3**.

In addition, the stabilization energy associated with the $LP_1O_{12}{\rightarrow}\sigma^*_{C2-M3}$ electron delocalization (*exo-AE*) for the axial conformations of compounds **1-3** are 13.50, 14.30 and 16.05 kcal mol^{-1} while for their equatorial conformations are 12.62, 12.72 and 14.43 kcal mol^{-1}, respectively. Also, the stabilization energy associated with the $LP_2O_{12}{\rightarrow}\sigma^*_{C2-M3}$ electron delocalization (*exo-AE*) for the axial conformations of compounds **1-3** are 0.73, 1.17 and 1.12 kcal mol^{-1} while for their equatorial conformations are 0.71, 0.80 and 0.80 kcal mol^{-1}, respectively.

Based on Eq. 2, the *AE* associated with The stabilization energies (E_2) associated with $LP_{ax}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$, $LP_{eq}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$ (*endo-AE*), $LP_1O_{12} \rightarrow \sigma^*_{C2\text{-}M3}$, $LP_2O_{12} \rightarrow \sigma^*_{C2\text{-}M3}$ (*exo-AE*) electron delocalizations for compounds **1-3** are -8.65, -10.72 and -9.42 kcal mol^{-1}, respectively. Based on the results obtained, the *AE* increases from compound **1** to compound **2** but decreases from compound **2** to compound **3**. Since the calculated $\Delta G_{ax\text{-}eq}$ increases from compound **1** to compound **2** but decreases from compound **2** to compound **3**, the rationalization of the conformational preference solely in terms of the *AE* succeeds to account for compounds **1-3**.

Table 2
Calculated resonance (stabilization) energies associated with donor-acceptor delocalizations, Anomeric Effects and dipole moments for the axial and equatorial conformations of the chair and boat forms of compounds **1-3**, using NBO analysis based on the optimized structures by B3LYP /6-311+G** level of theory.

	1		2		3	
	Eq	Ax	Eq	Ax	Eq	Ax
donor→acceptor						
$LP_1O_{12} \rightarrow \sigma^*_{C2\text{-}M3}$	0.71	0.73	0.80	1.17	0.80	1.12
$LP_2O_{12} \rightarrow \sigma^*_{C2\text{-}M3}$	12.62	13.50	12.72	14.30	14.43	16.05
$LP_{eq}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$	3.57	1.45	0.83	0.77	---	0.58
$LP_{ax}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$	1.39	11.26	---	8.83	---	6.90
Σ	18.29	26.94	14.35	25.07	15.23	24.65
AE	-8.65		-10.72		-9.42	
M (Debye)	1.6873	0.4279	1.8543	0.3744	1.7586	0.4710
$\Delta(\mu_{eq\text{-}ax})$	1.2594		1.4799		1.2876	
F_{ij}						
$LP_1O12 \rightarrow \sigma^*_{C2\text{-}M3}$	0.022	0.023	0.021	0.026	0.020	0.024
$LP_2O_{12} \rightarrow \sigma^*_{C2\text{-}M3}$	0.078	0.081	0.067	0.071	0.067	0.071
$LP_{eq}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$	0.050	0.031	0.025	0.024	---	0.022
$LP_{ax}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$	0.027	0.074	---	0.062	---	0.054
$\Delta E_{i,j}$						
$LP_1O_{12} \rightarrow \sigma^*_{C2\text{-}M3}$	0.84	0.86	0.69	0.69	0.63	0.63
$LP_2O_{12} \rightarrow \sigma^*_{C2\text{-}M3}$	0.59	0.60	0.44	0.44	0.38	0.39
$LP_{eq}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$	0.87	0.85	0.91	0.91	---	0.99
$LP_{ax}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$	0.63	0.61	---	0.53	---	0.52

3.3. Orbital occupancies

The NBO results showed that the $LP_{ax}M_3$ nonbonding orbital occupancies in the axial conformations of compounds **1-3** are 1.91048, 1.91175 and 1.92733, respectively (see Table 4). Also, the NBO results revealed that the $\sigma*_{C2-O12}$ antibonding orbital occupancies in the axial conformations of compounds **1-3** are 0.05814, 0.05739 and 0.05133, respectively. In addition, the LP_2O_{12} nonbonding orbital occupancies in the axial conformations of compounds **1-3** are 1.89904, 1.89261 and 1.88486 while the $\sigma*_{C2-O12}$ antibonding orbital occupancies are 0.06780, 0.08253 and 0.09414, respectively. This trend can be justified by the decrease of the $LP_{ax}M_3 \rightarrow \sigma*_{C2-O12}$ electron delocalization (*exo-AE*) and the increase of the $LP_2O_{12} \rightarrow \sigma*_{C2-M3}$ (*exo-AE*) from the axial conformations of compound **1** to compound **3**.

Table 3
NBO calculated non-bonding and anti-bonding orbital occupancies, based on the calculated geometries using B3LYP /6-311+G** level of theory, for the axial and equatorial conformations of the chair and boat forms of compounds **1**-**3**.

	LP_1O_{12}	LP_2O_{12}	$LP_{eq}M_3$	$LP_{ax}M_3$	$\sigma*_{C2-O12}$	$\sigma*_{C2-M3}$
Occupancy						
1-Eq	1.96352	1.90132	1.95247	1.92063	0.04061	0.06454
1-Ax	1.96470	1.89904	1.95814	1.91048	0.05814	0.06780
2-Eq	1.96318	1.90006	1.97805	1.93119	0.03301	0.07156
2-Ax	1.96065	1.89261	1.97873	1.91175	0.05739	0.08253
3-Eq	1.96274	1.89247	1.98512	1.94775	0.03083	0.08319
3-Ax	1.95976	1.88486	1.98495	1.92733	0.05133	0.09414

Table 4
NBO calculated non-bonding and anti-bonding orbital energies, based on the calculated geometries using B3LYP /6-311+G** level of theory, for the axial and equatorial conformations of the chair and boat forms of compounds **1**-**3**.

	LP_1O_{12}	LP_2O_{12}	$LP_{eq}M_3$	$LP_{ax}M_3$	$\sigma*_{C2-O12}$	$\sigma*_{C2-M3}$
Energy						
1-Eq	-0.54650	-0.29202	-0.54260	-0.30152	0.32817	0.29740
1-Ax	-0.55133	-0.29376	-0.53613	-0.29142	0.31528	0.30457
2-Eq	-0.55391	-0.30389	-0.61191	-0.22844	0.30283	0.13112
2-Ax	-0.54864	-0.30173	-0.60645	-0.22720	0.30239	0.13848
3-Eq	-0.55136	-0.30665	-0.68607	-0.21649	0.30754	0.07620
3-Ax	-0.54571	-0.30567	-0.68110	-0.21107	0.31003	0.08198

3.4. Orbital energies and off-diagonal elements

The stereoelectronic orbital interactions are anticipated to be more effective for the *anti* rather than the *syn* or *gauche* arrangement between the donor (LP) and acceptor ($\sigma*$) orbitals, and the stabilization should increase as the anti-bonding orbital $\sigma*$ energy decreases and the non-bonding

orbital LP energy increases. The energy differences between donor (E_{LPaxM3}) and acceptor ($E\sigma_{*C2-O12}$) orbitals [i.e. $\Delta(E_{\sigma*C2-O12} - E_{LPax\ M3})$] for the axial conformations of compounds **1-3** are 0.61, 0.53 and 0.52 a.u., respectively, as calculated by NBO analysis. Based on the results obtained, $\Delta(E_{\sigma*C2-O12} - E_{LPax\ M3})$] decreases from the axial conformations of compound **1** to compound **3**. It can be concluded that the strong donor nonbonding orbital of compound **3** (E_{LPaxM3}=-0.21107 a.u.) [compared to those in compounds **2** (E_{LPaxM3}=-0.22720 a.u.) and **1** (E_{LPaxM3}=-0.29142 a.u.)] may give rise to strong *endo-AE* (see Tables 3, 4). It should be noted that the decrease of the *orbital overlap* (S) [off-diagonal elements (F_{ij})] values for the $LP_{ax}M_3{\rightarrow}\sigma*_{C2-O12}$ electron delocalization (endo-*AE*) from the axial conformations of compound **1** to compound **3** could reduce the *AE* (see Table 2). Importantly, there is conflict between the F_{ij}, $\Delta(E_{acceptor} - E_{donor})$ for the endo-*AE* in the axial conformations of compounds **1-3**. Since the second order perturbation energy (E_2) is related to the F_{ij}, $\Delta(E_{acceptor} - E_{donor})$, it seems that in the axial conformations of compounds **1-3** the F_{ij} could affect and control the order of the stabilization energy associated with $LP_{ax}M_3{\rightarrow}\sigma*_{C2-O12}$ electron delocalization (*endo-AE*).

3.5. Dipole moments

There is a preference for the conformation with the smallest resultant dipole moment. Especially in the gas phase it is generally found that the conformation with the larger dipole moment has the larger electrostatic energy. Therefore, the conformation with the larger dipole moment has an increased overall energy [24]. Table 2 presents the calculated dipole moments for the axial and equatorial conformations of compounds **1-3**.

B3LYP/6-311+G** results showed that the dipole moments for the equatorial conformations of compounds **1-3** are larger than those in their axial conformations. Using the dipole moments obtained, a "Δ" parameter could be found as $\Delta(\mu_{eq}-\mu_{ax})$. The results obtained showed that the calculated dipole moment difference [$\Delta(\mu_{eq} - \mu_{ax})$] values between the axial and equatorial conformations increase from compound **1** to compound **2** but increase from compound **2** to compound **3**. The variation of the ΔG_{ax-ax} values between the axial and equatorial conformations of compounds **1-3** can be explained by the variation of the $\Delta(\mu_{eq} - \mu_{ax})$ values (see Tables 1, 2). Importantly, there is no conflict between the AE and $\Delta(\mu_{eq} - \mu_{ax})$.

3.6. Structural parameters

Representative structural parameters for the axial and equatorial conformations of compounds **1-3**, as calculated at the B3LYP/6-311+G** level of theory, are shown in Table 5. Although it is not expected, in principal, to obtain exactly the experimental values because of the differences in definition of bond length values [25], it is possible to carry out theoretical calculations, from which many properties and structures can be obtained with an accuracy that is competitive with experiments [25-29].

Consideration of the structures of compounds **1-3** gave evidence that in the axial conformations of these compounds, the σ_{C2-M3} bond lengths are significantly contracted compared to those in their equatorial conformations. The B3LYP/6-311+G** results showed that the σ_{C2-M3} bond lengths in the axial conformations of compounds **1-3** are 1.419, 1.857 and 2.020 Å, respectively, while the corresponding values in the equatorial conformations are 1.424, 1.871 and 2.032 Å, respectively (see Table 4). The shorter σ_{C2-M3} bond lengths in the axial conformations of compounds **1-3**, compared to those in their equatorial conformations, are the result of the $LP_{ax}M_3{\rightarrow}\sigma*_{C2-O12}$ electron delocalization (*endo-AE*).

Using the structural parameters obtained, "Δ" parameters could be found as $\Delta[r_{3-3(eq)}-r_{3-3(ax)}]$ and $\Delta[r_{2-13(ax)}-r_{2-13(eq)}]$. There is a direct correlation between the calculated *AE* and $\Delta[r_{3-3(eq)}-r_{3-3(ax)}]$ (see

Tables 2, 5). Consequently, the calculated $\Delta[r_{2-13(ax)}-r_{2-13(eq)}]$ parameters could be proposed as a criterion for the evaluation of the *AE* values in compounds **1-3**.

Table 5
B3LYP /6-311+G** calculated structural parameters for the axial and equatorial conformations of the chair and boat forms of compounds **1-3**.

Compound	1		2		3	
State	Eq	Ax	Eq	Ax	Eq	Ax
Bond lengths (Å)						
r_{1-2}	1.533	1.535	1.536	1.538	1.535	1.537
r_{2-3}	1.424	1.419	1.871	1.857	2.032	2.020
r_{3-4}	1.423	1.432	1.833	1.835	1.982	1.982
r_{4-5}	1.536	1.535	1.540	1.538	1.539	1.536
r_{5-6}	1.516	1.514	1.515	1.514	1.517	1.516
r_{6-7}	1.410	1.408	1.409	1.408	1.410	1.409
r_{7-1}	1.515	1.515	1.516	1.516	1.517	1.517
r_{7-8}	1.400	1.398	1.400	1.399	1.401	1.401
r_{8-9}	1.394	1.394	1.393	1.393	1.393	1.393
r_{9-10}	1.392	1.391	1.392	1.391	1.392	1.392
r_{10-11}	1.394	1.394	1.393	1.393	1.393	1.393
r_{11-6}	1.400	1.398	1.400	1.399	1.401	1.401
r_{2-12}	1.395	1.406	1.405	1.405	1.401	1.398
r_{12-13}	1.425	1.424	1.425	1.421	1.425	1.420
$\Delta[r_{3-4(eq)}-r_{3-4(ax)}]$	0.005		0.014		0.012	
$\Delta[r_{2-12(ax)}-r_{2-12(eq)}]$	0.011		0.000		-0.003	
Bond angles (°)						
θ_{1-2-3}	112.8	114.7	113.2	114.8	112.5	113.9
θ_{2-3-4}	115.9	117.5	101.7	103.3	99.6	100.9
θ_{3-4-5}	113.7	114.3	115.6	115.7	115.5	115.6
θ_{4-5-6}	115.3	114.5	114.7	114.2	114.6	114.2
θ_{5-6-7}	121.5	120.8	122.3	122.2	122.7	122.6
θ_{6-7-1}	121.9	121.2	122.6	122.5	122.9	122.8
θ_{7-1-2}	114.7	117.1	114.5	116.6	114.1	116.3
θ_{1-2-12}	107.2	108.2	107.7	108.0	108.3	108.5
$\theta_{2-12-13}$	114.6	114.3	115.2	115.2	115.3	115.4
θ_{12-2-3}	107.7	112.8	107.9	114.6	108.1	114.6
θ_{1-7-8}	119.3	119.7	118.6	118.6	118.3	118.4
θ_{6-7-8}	118.9	119.1	118.8	118.8	118.8	118.8
θ_{7-8-9}	121.6	121.4	121.8	121.8	121.8	121.8
θ_{8-9-10}	119.5	119.5	119.4	119.4	119.4	119.4
$\theta_{9-10-11}$	119.5	119.5	119.4	119.4	119.4	119.4
$\theta_{10-11-6}$	121.6	121.4	121.8	121.8	121.9	121.8
θ_{11-6-5}	119.5	120.1	118.8	118.9	118.6	118.6
θ_{7-6-11}	118.9	119.1	118.8	119.0	118.7	118.8
Torsion angles (°)						
$\phi_{1-2-3-4}$	73.3	64.8	62.3	56.6	57.9	52.6
$\phi_{2-3-4-5}$	-72.4	-69.9	-62.3	-60.8	-57.6	-56.0
$\phi_{3-4-5-6}$	77.2	80.3	85.3	86.5	85.6	86.6
$\phi_{4-5-6-7}$	-56.9	-57.5	-67.7	-67.1	-71.9	-71.5

Table 5
Continued

Compound	1		2		3	
State	Eq	Ax	Eq	Ax	Eq	Ax
$\phi_{5-6-7-1}$	-0.2	-3.0	-0.2	-2.7	-0.011	-2.2
$\phi_{6-7-1-2}$	58.2	60.4	70.0	70.9	74.7	75.4
$\phi_{7-1-2-3}$	-79.1	-74.2	-86.8	-81.9	-87.8	-83.3
$\phi_{7-1-2-12}$	162.5	52.6	154.0	47.4	152.9	45.7
$\phi_{1-2-12-13}$	-174.7	166.0	-162.5	162.3	-162.3	163.1
$\phi_{13-12-2-3}$	63.6	-66.1	75.0	-68.4	75.6	-68.3
$\phi_{12-2-3-4}$	-168.5	-59.6	-178.5	-69.2	177.4	-73.2
$\phi_{5-6-7-8}$	179.9	178.7	179.6	178.7	179.5	179.0
$\phi_{6-7-8-9}$	0.2	0.2	-0.03	0.1	-0.9	-0.002
$\phi_{7-8-9-10}$	-0.2	-0.02	0.05	0.06	0.08	0.12
$\phi_{8-9-10-11}$	-0.01	-0.2	-0.01	-0.2	0.03	-0.08
$\phi_{9-10-11-6}$	0.1	0.2	-0.1	0.1	-0.1	-0.1
$\phi_{10-11-6-5}$	180.0	-178.9	-179.6	-178.8	-179.4	-179.0
$\phi_{10-11-6-7}$	-0.1	-0.04	0.1	0.1	0.1	0.2
$\phi_{11-6-7-8}$	-0.1	-0.2	-0.03	-0.2	-0.03	-0.14
$\phi_{11-6-5-4}$	123.0	121.3	112.0	-178.8	107.7	107.7
$\phi_{11-6-7-1}$	179.8	178.1	-179.8	178.4	-179.6	178.6
$\phi_{9-8-7-1}$	-179.7	-178.1	179.8	-178.5	179.5	-178.8
$\phi_{8-7-1-2}$	-121.9	-121.4	-109.8	-110.5	-104.8	-105.9

Also, the calculated $\Delta[r_{2-12(ax)}-r_{2-12(eq)}]$ values decrease from compound **1** to compound **3** (see Table 5). The decrease of the calculated $\Delta[r_{2-12(ax)}-r_{2-12(eq)}]$ values can be justified by the increase of the $LP_2O_{12}\rightarrow\sigma^*_{C2-M3}$ electron delocalization from the axial conformations of compound **1** to compound **3**.

4. Conclusions

The results of the hybrid density functional based method (DFT: B3LYP/6-311+G**) reported above and NBO analysis provided a reasonable picture from energetic, structural, bonding and stereoelectronic points of view for the conformational preference in compounds **1-3**. Effectively, the B3LYP/6-311+G** results showed that the calculated ΔG_{eq-ax} (axial conformation stability) increases from compound **1** to compound **2** but increases from compound **2** to compound **3**. In addition, NBO results revealed that

- similar to the trend observed for the variation of the ΔG_{eq-ax}, the *AE* increases from compound **1** to compound **2** but decreases from compound **2** to compound **3**.
- the rationalization of the conformation preference solely in terms of the *AE* succeeds to account quantitatively for the conformation preferences in compounds **1-3**.
- the increase of the $LP_{ax}M_3$ nonbonding and the decrease of the σ^*_{C2-O12} antibonding orbital occupancies in the axial conformations of compounds **1-3** can be justified by the decrease of the $LP_{ax}M_3\rightarrow\sigma^*_{C2-O12}$ electron delocalization (*exo-AE*) from the axial conformations of compound **1** to compound **3**.
- in the axial conformations of compounds **1-3** the F_{ij} could affect and control the order of the stabilization energy associated with $LP_{ax}M_3\rightarrow\sigma^*_{C2-O12}$ electron delocalization (*endo-AE*).
- the rich acceptor antibonding orbital of compound **3** and compound **6**, compared to those in compounds **1** and **2** and compounds **4** and **5** gives rise to strong *endo- AE*.
- The variation of the ΔG_{ax-ax} values between the axial and equatorial conformations of compounds **1-3** can be explained by the variation of the $\Delta(\mu_{eq} - \mu_{ax})$ values.

Also, the significantly contraction of the $\sigma_{C2\text{-}M3}$ bond lengths in the axial conformations of compounds **1**-**3** compared to those in their equatorial conformations are the result of the $LP_{ax}M_3 \rightarrow \sigma^*_{C2\text{-}O12}$ electron delocalization (*endo-AE*). The decrease of the calculated $\Delta[r_{2\text{-}3(ax)}\text{-}r_{2\text{-}3(eq)}]$ values can be justified by the increase of the $LP_2O_{12} \rightarrow \sigma^*_{C2\text{-}M3}$ electron delocalization from the axial conformations of compound **1** to compound **3**. Importantly, the calculated $\Delta[r_{2\text{-}3(ax)}\text{-}r_{2\text{-}3(eq)}]$ parameters could be proposed as a criterion for the evaluation of the *AE* values in compounds **1**-**3**.

References

[1] T. Edwards, Chem. Ind. (London) (1955) 1102.

[2] N.D. Epiotis, R.L. Yates, R.J. Larson, C.R. Kirmayer, F. Bernardi, J. Am. Chem. Soc. 99 (1977) 8379-8388.

[3] E.L. Eliel, S.H. Wilen, Stereochemistry of Organic Compounds, Wiley, New York, 1994.

[4] E. Juaristi, G. Cuevas, The Anomeric Effect, CRC Press. Inc., Florida, 1995.

[5] N.L. Allinger, J. A. Hirsch, M.A. Miller, F.A. VanCatledge, J. Am. Chem. Soc. 90 (1968) 1199-1210.

[6] J.–P. Praly, R.U. Lemieux, Can. J. Chem. 65 (1987) 213-223.

[7] S. Désilets, M. St-Jacques, Can. J. Chem. 70 (1992) 2650-2657.

[8] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery, T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian 03, Revision B.03, Gaussian, Inc., Wallingford CT, 2004.

[9] A.D. Becke, J. Chem. Phys. 98 (1993) 5648-5652.

[10] C. Lee, W. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785-789.

[11] W.J. Hehre, L. Radom, P.v.R. Schleyer, J.A. Pople, Ab initio Molecular Orbital Theory, Wiley, New York, 1986.

[12] J.M. Seminario, P. Politzer, (Eds), Modern Density Function Theory, A Tool for Chemistry, Elsevier, Amsterdam, 1995.

[13] E.D. Glendening, J.K. Badenhoop, A.E. Reed, J.E. Carpenter, J.A. Bohmann, C.M. Morales, F. Weinhold, Theoretical Chemistry Institute, University of Wisconsin, Madison, WI, 2004. NBO Version 5.G.

[14] N.D. Epiotis, R.L. Yates, R.J. Larson, C.R. Kirmayer and F. Bernardi, J. Am. Chem. Soc. 99 (1977) 8379-8388.

[15] P. Dionne, M. St-Jacques, J. Am. Chem. Soc. 109 (1987) 2616-2623.

[16] F. Weinhold, Angew. Chem. Int. Ed. 42 (2003) 4188-4194.

[17] D. Nori-Shargh, F. Roohi, F. Deyhimi, R. Naeem-Abyaneh, J. Mol. Struct. (THEOCHEM) 763 (2006) 21-28.

[18] D. Nori-Shargh, M. Malekhosseini, F. Deyhimi, J. Mol. Struct. (THEOCHEM) 763 (2006) 187-198.

[19] D. Nori-Shargh, F. Deyhimi, J.E. Boggs, S. Jameh-Bozorghi, R. Shakibazadeh, J. Phys. Org. Chem. 20 (2007) 355-364.

[20] D. Nori-Shargh, H. Yahyaei, J. Mol. Struct. (THEOCHEM) 913 (2009) 8-15.

[21] D. Nori-Shargh, N. Hassanzadeh, M. Kosari, S. Sharifi, J. Mol. Struct. (THEOCHEM) 940 (2010) 129-134.

[22] A. Zeinalinezhad, D. Nori-Shargh, Z. Abbasi-Bakhtiari, J.E. Boggs, J. Mol. Struct. (THEOCHEM) 947 (2010) 52-57.

[23] D. Nori-Shargh, H. Yahyaei, J.E. Boggs, J. Mol. Graph. Model. 91 (2010) 3616-3620.

[24] D. Nosi-Shargh, Z. Mahmoodi, N. Masnabadi, H. Yahyaei, S.N. Mousavi, J. Iran. Chem. Res. 3 (2010) 179-189.

[25] F. Freeman, A. Phornvoranunt, W.J. Hehre, J. Phys. Org. Chem. 11 (1998) 831-839.

[26] T.M. Gilbert, Tetrahedron Lett. 39 (1998) 9147-9150.

[27] M. Remko, P.D. Lyne, W.G. Richards, Phys. Chem. Chem. Phys. (1991) 5353-5357.

[28] D. Strickland, R.A. Caldwell, J. Phys. Chem. 97 (1993) 13394-13402.

[29] I. Arnason, G.K. Thorarinson, E. Matern, J. Mol. Struct. (THEOCHEM) 454 (1998) 91-102.